REMARKS

With this Amendment, claims 29 and 33 have been amended and new Claims 49-79 have been added. As will be discussed in more detail below, the amendments recite with greater clarity and particularity certain features of Applicants' invention and are believed to be in condition for allowance. Applicants reserve the right to prosecute claims drawn to canceled subject matter in one or more continuation, divisional, or continuation-in-part applications. For the Examiner's convenience a copy of the claims as pending after entry of this Amendment is attached hereto as Exhibit A.

I. AMENDMENTS TO THE SPECIFICATION

The specification has been amended to correct minor typographical errors; the amendments do not entail the introduction of new matter. These amendments are fully supported by the application and the claims as originally filed.

In a Preliminary Amendment (filed November 17, 1997), Applicants requested that the specification be amended at page 28, line 26, to insert --(SEQ ID NO:11)-- after "was". (Preliminary Amendment, page 1, second line from bottom of page to page 2, line 2). However, in a subsequent Amendment Under 37 C.F.R. § 1.111 (filed April 26, 1999), Applicants requested that the previous insertion of --(SEQ ID NO:11)-- be deleted by stating "On page 28, line 36, please delete '(SEQ ID NO:11)'" (Amendment Under 37 C.F.R. § 1.111 filed April 26, 1999, page 3, fifth line from the bottom of the page, emphasis added). "36" is a typographical error; the phrase to be deleted occurs at line 26. Applicants therefore respectfully request that the specification be amended to delete "(SEQ ID NO:11)" at page 28, line 26.

In the Amendment filed April 26, 1999, Applicants requested that "[f]ollowing insertion of Table 1, on page 33, line 25, following "INS", please insert --(SEQ ID NO:24)--." (Amendment Under 37 C.F.R. § 1.111 filed April 26, 1999, page 5, next-to-last and last lines from bottom of page, emphasis added). "INS" is a typographical error; "DEL," rather than "INS," appears on page 33 at line 25. Applicants therefore respectfully request that following insertion of Table 1, that --(SEQ ID NO:24)-- be inserted following "DEL" on page 33, line 25.

II. AMENDMENTS TO THE CLAIMS

With this Amendment Claims 29 and 33 have been amended and new Claims 49-79 have been added. The amendments clarify the claimed compositions. No new matter is added by virtue of these amendments. Claims 29 and 33 have been amended to clarify that the polynucleotides that they recite are for diagnosing hereditary hemochromatosis. These amendments find support in the Specification at, for example, page 12, lines 21-33, page 14, line 27 through page 15, line 22 and page 27, line 30 through page 29, line 16. New Claims 49-54 and 69-74 find support in the Specification at, for example, page 11, line 25 through page 12, line 10, page 12, lines 32-33, page 3, lines 29-33, page 13, lines 30-35, Table 1, Figures 1 and 2 and Claims 1-4 and 26 as originally filed.[1] New Claims 55-60 and 75-79 find support in the Specification at, for example, page 11, line 25 through page 12, line 10, page 12, lines 32-33, page 14, line 5, page 16, lines 10-13, Table 1 and Figures 1 and 2.[2] New

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[1] Claim 69, from which Claims 70-74 depend, recites all of the polymorphisms of Table 1 except for the polymorphisms found at positions 35-36; 32,512-32,559; 53,631-53,637; 178,551-178,552; 214,529-214,530 and 225,366-225,367.

[2] Claim 75, from which Claims 76-79 depend, recites all of the polymorphisms (continued...)

Claims 61-64 find support in the Specification at, for example, page 11, line 25 through page 12, line 10, page 12, lines 32-33, page 14, line 1, Table 1 and Figures 1 and 2. New Claims 65-68 find support in the Specification at, for example, page 10, line 34, page 11, line 25 through page 12, line 10 page 14, line 1, Table 1 and Figures 1 and 2. Accordingly, entry thereof is respectfully requested.

III. VERSION WITH MARKINGS TO SHOW CHANGES MADE

Paragraph beginning at page 28, line 26:

The phosphorylated digoxigenin-labeled primer used was [(SEQ ID NO:11)]:

182. 1G7 .D 5' (p) AGAAGAGATAGATATGGTGG - 3' (SEQ ID NO:11)

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Page 30 (version with markings to show changes made) appears on the next page.

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[2] (...continued)
of Table 1 except for the polymorphisms found at positions 35-36; 32,512-32,559; 53,631-53,637; 178,551-178,552; 214,529-214,530 and 225,366-225,367.

Table 1A. Polymorphic Sites in the HH Region

BASE LOCATION	DIFFERENCE	BASE LOCATION	DIFFERENCE
3336	[AC] AC DEL	20463	C-A
2661	T-C	20841	A-T
2662-2663	TT DEL	21059	A-T
3767	T-C	21117	A-G
3829	C-G	21837	A-C
4925-4928	TAAA DEL	22293	A-C
5691	C-T	22786	C-A
5839	T-C	23009	G-A
6011	G-A	24143	T-A
6047	C-G	26175	G-C
6231	G-A	26667	C-A
6643	A DEL	26994	T-C
6698	T-C	27838	G-T
7186	T-C	27861	T DEL
7273	G-A	28132	G-A
7545-7558	TCACACACCGATTGG DEL (SEQ ID NO:17)	29100	G-A
7672	G DEL	29454-29457	TTTT DEL
7933	T-C	29787	T-G
8746	T-G	29825	A-C
9115	G-A	30009	T-C
9823	G-A	30177	A-G
10027	G-A	30400	A-G
10214	C-T	31059	T-A
10828	A-G	31280	C-T
10918	C-G	31749	C-T
10955	A-G	32040	C-G
11524	C-A	[32556-32559] 32534-32537	[TGTG] GTGT DEL
11674	A-G	33017	T-G
11955	T-C	33026	T DEL
12173-12175	TTT DEL	34434	C-T
13304	G-A	35179	A-C
13455	G-A	35695	G-A
14416-14417	A INS	35702	G-A
14998	C-T	35983	A-G
15564	T-C	37411	A-G
15887	A-G	38526	C-T
15904-1 5919	CCAAACTGATCTTTGA DEL (SEQ ID NO:18)	40431	C-A
16019	T DEL	42054-42055	TT DEL
16211	A-T	43783-43784	TTTT INS
17461	A-G	45120	C DEL
19755	G-A	45567	A-C
19949	C-T	46601	A-T
20085	C-T	47255	C-G
20366-20367	A INS		

NEW MATTER

Page 33 (version with markings to show changes made) appears on the next page.

Table 1D. Polymorphic Sites in the HH Region.

BASE LOCATION	DIFFERENCE	BASE LOCATION	DIFFERENCE
176684	A-T	193499	C-T
176684-176684	G-A	193738	C-G
176815	T-C	193984-193985	ACACACAC INS
177049	T-C	194064	C-G
177065	G-T	194504	A DEL
178285	T-C	194734	G-A
178551-178552	CTTTTTTTTTTTT INS (SEQ ID NO: 23)	194890	A-C
179114-179115	A INS	195404	G-A
179260	C-G	195693	A-T
179281	C-G	196205	G-A
180023	G-C	197424	C-T
180430	T-C	197513	C-T
180773	T-C	197670	G-A
180824	T-C	198055	C-A
181097	C-T	198401	C-T
181183	A-T	198692	A-G
182351	C-T	198780	T DEL
183197	G-A	199030	T-G
183623	A-T	199933	C-T
183653	G-T	200027	G-A
183657	T-G	200439	T-A
183795-183796	A INS	200452	A-G
184060	G-A	200472-200483	AATAATAATAAT DEL (SEQ ID NO: 24)
184993	G-A	200559	A-T
185918	A-G	200745	A-G
186036	T-C	200919	T-A
186506-186507	TAAC INS	201816	C-T
186561-186568	TATTTATT DEL	201861-201862	42bp INS
186690	G DEL	202662	T-C
186751	T-A	202880	T-C
187221	A-G	204341	C-T
187260	A-G	204768	A-T
187444-187447	CTCT DEL	205284	T-G
187831-187832	C INS	207400	C-A
188638	G-A	208634	T-C
188642	C-T	208718	T DEL
189246	T-C	208862	A-C
190340	A-C	209419-209420	TT DEL
190354	A-G	209802	G-A
190762	A-G	209944	C-G
191260	G-T	210299	A-G
193018-193019	AGAT INS	211142	G-A
193147	T-G	212072	G-A
193196-193197	C INS	212146	T-C

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IV. CLAIM REJECTIONS

A. Rejection of Claims 29-48 Under Nonstatutory Obviousness-Type Double Patenting Doctrine

Claims 37-44 stand rejected over Claim 1 of U.S. Patent No. 5,872,237 ("the '237 [illegible]"), and Claims 29-48 stand rejected over Claim 1 of the '237 patent in view of Campbell *et al.*, 1985, Monoclonal Antibody Technology (Campbell, ed.), Elsevier Science Publishers, under the judicially created doctrine of obviousness-type double patenting. Without agreeing with the propriety of this rejection, and solely to expedite prosecution of the instant Application, Applicants file herewith a terminal disclaimer with respect to the '237 patent, rendering the instant rejection moot. Accordingly, Applicants respectfully request that this rejection be withdrawn.

B. Rejection of Claims 29-48 Under 35 U.S.C. § 112, First Paragraph

Claims 29-48 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking adequate written description. The instant rejection is respectfully traversed with respect to Claims 29-48, and inapposite with respect to new Claims 49-79.

Legal standard. An Applicant's disclosure satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, if it "convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, [the Applicant] was in possession of *the invention*." *Vas-Cath Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991) (emphasis in original). The invention is whatever is now claimed. *See id.*

The courts have repeatedly emphasized that written description is a fact-specific issue. *See id.* at 1116 ("the precedential value of cases in this area [*i.e.*, written description] is extremely limited" quoting *In re Driscoll*, 195 U.S.P.Q. 434, 438 (C.C.P.A. 1977)). Thus, it

is necessary to consider the specific facts of the cases cited by the Examiner as supporting a finding of lack of written description and compare them with the facts of the instant case.

The Examiner cites several cases that interpret the written description requirement as it pertains to nucleic acids. In *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993) the court considered whether a Specification teaching a method of isolating a fragment of a gene and a method of isolating an mRNA encoding the gene, but not the sequence of the gene or its mRNA, provided adequate written description for an interference count reading "[a] DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide." In *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), the court considered whether conception of a purified and isolated DNA sequence encoding human erythropoietin was established when the inventor conceived of a method of isolating the gene or when the inventor actually isolated the gene. In *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997), the court considered whether a Specification disclosing only the sequence of a rat insulin cDNA provided adequate written description for claims directed generally to all vertebrate or mammalian insulin cDNAs.

The facts of the instant case are immediately distinguishable from the facts relied on by the court in *Fiers* and *University of California*. The Specification in *Fiers* taught only a *method* of isolating a gene, not the sequence of the gene. The court held that a plan or scheme for isolating a gene *by itself* does not provide written description for the gene. In the instant case, Applicants provide approximately 470 kilobases of sequence information in Figures 1 and 2. All of the claimed polynucleotides comprise or consist of portions of the sequence of Figure 1 or 2. Moreover, the rejected claims of the instant application recite *genera* of nucleic acids, an issue that *Fiers* does not address. *Amgen* concerns the requirement for establishing *conception* and so is not directly controlling in the instant case.

Furthermore, like *Fiers*, *Amgen* is inapposite because it concerns the adequacy of a disclosed *method* of isolating a nucleic acid to provide written description for a *single* claimed nucleic acid.

Although *University of California* involves a claimed genus of nucleic acids, it is nonetheless clearly distinguishable from the instant case. The court found the disputed patent's written description inadequate because

> it does not distinguish the claimed genus from others, except by function[, i]t does not specifically define any of the genes that fall within its definition [, and i]t does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize *or recognize* the identity of the members of the genus.

University of California, 43 U.S.P.Q.2d at 1406 (emphasis added). Applicants' Specification overcomes each of the shortcomings identified by the court: Applicants' claimed genera are distinguished from others by function (*i.e.*, diagnosis of hereditary hemochromatosis) *and specifically defined structural features* (*i.e.*, the sequences disclosed in Figures 1 and 2, the polymorphisms of Table 1 and the length ranges appearing in the Specification *passim*). Consequently, one of skill in the art can *recognize* all of the members of each of Applicants' claimed genera. Thus, Applicants have satisfied the written description requirement as it is formulated in *University of California*. Applicants therefore respectfully request that the instant rejection be withdrawn.

D. Rejections of Claims 29, 33, 45 and 46 Under 35 U.S.C. § 102

Claims 29, 33, 45 and 46 stand rejected under 35 U.S.C. 102(b) as being allegedly anticipated by Cornall *et al.*, 1991, Genomics 10:874-81 ("Cornall"). Claims 29, 33, 45 and 46 also stand rejected under 35 U.S.C. 102(a,e) as being allegedly anticipated by U.S. Patent No. 5,582,979 to Weber ("the '979 patent"). Claims 29, 33, 45 and 46 further stand rejected

under 35 U.S.C. 102(a,e) as being allegedly anticipated by U.S. Patent No. 5,719,125 to Suzuki *et al.* ("the'125 patent").

Each of these rejections is traversed with respect to Claims 29, 33, 45 and 46, and inapposite to new Claims 49-79.

The Legal Standard. The standard governing anticipation under 35 U.S.C. § 102 is one of strict identity. Anticipation can only be established by a prior art reference if it discloses *each and every element* of the claimed invention either explicitly or impliedly; there must be no difference between the invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *See Scripps Clinic & Research Foundation, Inc. v. Genentech*, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991); MPEP § 706.02.

The Claimed Invention. The independent polynucleotide claims of the instant Application can be divided into four groups. The first group of independent claims, Claims 29 and 33, recite polynucleotides for diagnosing hereditary hemochromatosis comprising portions of the sequences of SEQ ID NOs:1 and 2 and one or more polymorphisms of Table 1. The second group of independent claims, Claims 37 and 41, recite polynucleotides comprising portions of the sequences of SEQ ID NOs:1 and 2 and one or more polymorphisms of Table 1. The third group of independent claims, Claims 49, 55, 61 and 65, recite polynucleotides consisting of portions of the sequences of SEQ ID NOs:1 and 2 and one or more polymorphisms of Table 1. The fourth group of independent claims, Claims 69 and 75, recite polynucleotides comprising a portion of the sequences of SEQ ID NOs:1 and 2 and one or more polymorphisms recited in the claim. As will be explained in more detail below, none of these claims (or the claims depending therefrom) is anticipated by the cited art.

Rejection of Claims 29, 33, 45 and 46 Under 35 U.S.C. § 102(b)

Claims 29, 33, 45 and 46 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Cornall. Applicants respectfully traverse.

In Table 1, Cornall teaches randomly generated $(CA)_n$ microsatellite variants in the mouse including sequence #22, a 90-base sequence[3] comprising $(CA)_{23}$ nnn:[4]

Sequence Number	Locus	$(CA)_n$	GenBank Accession (GI) Number	Deposited Sequence
22	D16Nds2	$(CA)_{23}$	50729	attggtgagc ttacagaata cacacacaca cacacacaca cacacacaca cacacacaca cacacannna tctacgaata tcatgaccac

Amended Claims 29 and 33, from which Claims 45 and 46 depend, recite polynucleotides for diagnosing hereditary hemochromatosis. SEQ ID NO:1 discloses a $(CA)_{18}$ repeat at nucleotides 1-36. SEQ ID NO:2 discloses a $(CA)_{17}$ repeat in the same location. As one of skill in the art guided by Applicants' disclosure would appreciate, the 90-base sequence comprising a $(CA)_{23}$ repeat taught by Cornall cannot be used to distinguish a $(CA)_{18}$ repeat from a $(CA)_{17}$ repeat, much less diagnose hereditary hemochromatosis. Thus, Applicants respectfully request that this rejection be withdrawn.

Nor is this rejection apposite to the new claims. The sequence of the oligonucleotide taught by Cornall diverges from that disclosed in SEQ ID NOs:1 and 2 outside of the $(CA)_{18}$ repeat or $(CA)_{17}$ repeat, respectively. New Claims 49, 55, 61 and 65 recite polynucleotides *consisting of* sequences encompassed by the sequences of SEQ ID NOs:1 and 2. The CA

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[3] Applicants believe that the Examiner inadvertently referred to this as a 97-base sequence in the Office Action.

[4] Cornall indicates that sequence #22 comprises $(CA)_{23}$ but does not provide the full 90-base sequence. The GenBank accession number and full sequence #22 were downloaded from GenBank at http://www.ncbi.nlm.nih.gov.

polymorphism at position 35-36 of SEQ ID NO:1 is not included in the chart of polymorphisms recited in new Claims 69 and 75.[5] Thus, the instant rejection is inapposite to new Claims 49, 55, 69 and 75.

2. Rejection of Claims 29, 33, 45 and 46 Under 35 U.S.C. § 102(a,e)

Claims 29, 33, 45 and 46 stand rejected under 35 U.S.C. 102(a,e) as being allegedly anticipated by the '979 patent. The '979 patent teaches polynucleotides 300 base pairs or shorter in length containing one or more blocks of $(CA)_n$•$(GT)_n$ tandem repeats. One of these sequences, a 44-base oligonucleotide, SEQ ID NO: 249, allegedly comprises positions 1-38 of SEQ ID NO: 1 and the polymorphic site of Table 1 located at nucleotide position 35-36. Another of these sequences is a 56-base oligonucleotide, SEQ ID NO: 149. It allegedly comprises positions 32512-32559 of SEQ ID NO: 1 and the polymorphic site of Table 1 located at nucleotide position 32556-32559.[6] As explained above, amended Claims 29 and 33 recite polynucletides for diagnosing hereditary hemochromatosis, which the oligonucleotide of SEQ ID NOs:249 and 149 are incapable of. Furthermore, neither SEQ ID NO:249 or 149 *consists of* sequences encompassed by the sequences of Figures 1 or 2, thus they are not claimed by new Claims 49, 55, 61 or 65. The polymorphisms at position 35-36 and 32556-32559 of SEQ ID NO:1 are not among the polymorphisms recited in new Claims 69 and 75. Thus, rejection under SEQ ID NO:249 or 149 of the '979 patent is inapposite to new Claims 49-79.

INTENDED

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[5] As explained above, the description of this polymorphic site in Table 1 contains an error. It is actually a CA deletion.

[6] As explained above, the description of this polymorphic site in Table 1 contains two errors. It is actually a GTGT deletion of residues 32534-32537 of SEQ ID NO:1.

3. Rejection of Claims 29, 33, 45 and 46 Under 35 U.S.C. § 102(a,e)

Claims 29, 33, 45 and 46 stand rejected under 35 U.S.C. § 102(a,e) as allegedly being anticipated by the '125 patent. The Examiner asserts that the '125 patent teaches a 60-base oligonucleotide, SEQ ID NO: 11, which comprises the polymorphic sites of Table 1 located at nucleotide positions 53631-53637, 178551-178552, 214529-214530 and 225366-225367. The instant rejection is traversed with respect to amended Claims 29, 33, and Claims 45 and 46, and inapposite to new Claims 49-79.

The '125 patent teaches the polynucleotide SEQ ID NO: 11:

CTCGAGGCCA TGGCGGCCGC $(T)_{40}$

The polymorphic sites allegedly encompassed by this sequence are listed in the following chart.

Polymorphic Site	Polymorphism	Polymorphic Allele in SEQ ID NO:1	Polymorphic Allele in SEQ ID NO:2
53631-53637	$(T)_7$ deletion	$(T)_{37}$	$(T)_{30}$
178551-178552	$C(T)_{13}$ insertion	$(T)_{12}$	$C(T)_{25}$
214529-214530	$(T)_{11}$ insertion	$(T)_{28}$	$(T)_{39}$
225366-225367	$(T)_4$ insertion	$(T)_{23}$	$(T)_{27}$

INTENDED USE

As explained above, amended Claims 29 and 33 recite polynucleotides for diagnosing hereditary hemochromatosis. The $(T)_{40}$ sequence of SEQ ID NO:11 cannot distinguish between the polymorphic alleles of the polymorphic sites listed in the chart above, much less diagnose hereditary hemochromatosis. Thus, SEQ ID NO:11 does not anticipate Claims 29, 33, 45 or 46. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Nor is this rejection apposite to the new polynucleotide claims. SEQ ID NO:11 of the '125 patent does not *consist of* sequences encompassed by the sequences of SEQ ID NO:1 or

2 of the instant Application, thus it is not claimed by new Claims 49, 55, 61 or 65. The polymorphisms of the above chart are not recited in new Claims 69 and 75. Thus, rejection under SEQ ID NO:249 or 149 of the '979 patent is inapposite to new Claims 49-79

CONCLUSION

Applicants respectfully request that the above-made amendments and remarks be considered and made of record in the file history of the instant application. Applicants submit that Claims 29-79, as amended, meet all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore respectfully requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date January 31, 2001

42,067
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Exhibit A

Claims Pertaining After Entry Of The Instant Amendments

29. (Twice Amended) An isolated polynucleotide for diagnosing hereditary hemochromatosis comprising at least 8 consecutive bases and up to about 100 consecutive bases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

30. (Amended) The isolated polynucleotide of Claim 29, wherein the polymorphic site is at base 61465 of SEQ ID NO:1.

31. (Amended) The isolated polynucleotide of Claim 29, wherein the polymorphic site is at base 35983 of SEQ ID NO:1.

32. (Amended) A pair of isolated polynucleotides as in Claim 29.

33. (Twice Amended) An isolated polynucleotide for diagnosing hereditary hemochromatosis comprising at least 18 consecutive bases and up to about 100 consecutive bases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

34. (Amended) The isolated polynucleotide of Claim 33, wherein the polymorphic site is at base 61465 of SEQ ID NO:1.

35. (Amended) The isolated polynucleotide of Claim 33, wherein the polymorphic site is at base 35983 of SEQ ID NO:1.

36. (Amended) A pair of isolated polynucleotides as in Claim 33.

37. (Amended) An isolated polynucleotide comprising a fragment of at least about 100 consecutive bases and up to about 235 consecutive kilobases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

38. (Amended) The isolated polynucleotide of Claim 37 which is cDNA.

39. (Amended) The isolated polynucleotide of Claim 37 which is RNA.

40. (Amended) The isolated polynucleotide of Claim 37 which is genomic DNA.

41. (Amended) An isolated polynucleotide comprising a fragment of at least about 300 consecutive bases and up to about 235 consecutive kilobases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

42. (Amended) The isolated polynucleotide of Claim 41 which is cDNA.

43. (Amended) The isolated polynucleotide of Claim 41 which is RNA.

44. (Amended) The isolated polynucleotide of Claim 41 which is genomic DNA.

45. (Amended) A kit comprising an isolated polynucleotide of Claim 29.

46. (Amended) A kit comprising an isolated polynucleotide of Claim 33.

47. (Amended) A kit comprising at least one pair of isolated polynucleotides as in Claim 32.

48. (Amended) A kit comprising at least one pair of isolated polynucleotides as in Claim 36.

49. (New) An isolated polynucleotide consisting of at least 8 consecutive bases and up to about 100 consecutive bases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

50. (New) The isolated polynucleotide of Claim 49, wherein the polymorphic site is at base 61465 of SEQ ID NO:1.

51. (New) The isolated polynucleotide of Claim 49, wherein the polymorphic site is at base 35983 of SEQ ID NO:1.

52. (New) A pair of isolated polynucleotides as in Claim 49.

53. (New) A kit comprising an isolated polynucleotide of Claim 49.

54. (New) A kit comprising at least one pair of isolated polynucleotides as in Claim 52.

55. (New) An isolated polynucleotide consisting of at least 18 consecutive bases and up to about 100 consecutive bases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

56. (New) The isolated polynucleotide of Claim 55, wherein the polymorphic site is at base 61465 of SEQ ID NO:1.

57. (New) The isolated polynucleotide of Claim 55, wherein the polymorphic site is at base 35983 of SEQ ID NO:1.

58. (New) A pair of isolated polynucleotides as in Claim 55.

59. (New) A kit comprising an isolated polynucleotide of Claim 55.

60. (New) A kit comprising at least one pair of isolated polynucleotides as in Claim 58.

61. (New) An isolated polynucleotide consisting of a fragment of at least about 100 consecutive bases and up to about 235 consecutive kilobases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

62. (New) The isolated polynucleotide of Claim 61 which is cDNA.

63. (New) The isolated polynucleotide of Claim 61 which is RNA.

64. (New) The isolated polynucleotide of Claim 61 which is genomic DNA.

65. (New) An isolated polynucleotide consisting of a fragment of at least about 300 consecutive bases and up to about 235 consecutive kilobases of the sequence shown in SEQ ID NOS:1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site shown in Table 1.

66. (New) The isolated polynucleotide of Claim 65 which is cDNA.

67. (New) The isolated polynucleotide of Claim 65 which is RNA.

68. (New) The isolated polynucleotide of Claim 65 which is genomic DNA.

69. (New) An isolated polynucleotide comprising at least 8 consecutive bases and up to about 100 consecutive bases of the sequence shown in SEQ ID NOS: 1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site selected from the group consisting of polymorphic sites listed in the following table:

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
841	T-C
2662-2663	TT DEL
3767	T-C
3829	C-G
4925-4928	TAAA DEL
5691	C-T
5839	T-C
6011	G-A
6047	C-G
6231	G-A
6643	ADEL
6698	T-C
7186	T-C
7273	G-A
7545-7558	TCACACACCGATTGG DEL (SEQ ID NO:17)
7672	G DEL
7933	T-C

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
8746	T-G
9115	G-A
9823	G-A
10027	G-A
10214	C-T
10828	A-G
10918	C-G
10955	A-G
11524	C-A
11674	A-G
11955	T-C
12173-12175	TTT DEL
13304	G-A
13455	G-A
14416-14417	A INS
14998	C-T
15564	T-C
15887	A-G
15904-1 5919	CCAAACTGATCTTTGA DEL (SEQ ID NO:18)
16019	T DEL
16211	A-T
17461	A-G
19755	G-A
19949	C-T
20085	C-T
20366-20367	A INS
20463	C-A
20841	A-T
21059	A-T
21117	A-G
21837	A-C
22293	A-C
22786	C-A
23009	G-A
24143	T-A
26175	G-C
26667	C-A
26994	T-C
27838	G-T
27861	T DEL
28132	G-A
29100	G-A
29454-29457	TTTT DEL
29787	T-G
29825	A-C
30009	T-C
30177	A-G
30400	A-G
31059	T-A
31280	C-T
31749	C-T
32040	C-G
33017	T-G

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
33026	T DEL
34434	C-T
35179	A-C
35695	G-A
35702	G-A
35983	A-G
37411	A-G
38526	C-T
40431	C-A
42054-42055	TT DEL
43783-43784	TTTT INS
45120	C DEL
45567	A-C
46601	A-T
47255	C-G
47758	C-A
47994	G-C
48440	G-A
48650	T-G
48680	A-G
50240	C-T
50553	G-A
50586	G-T
51322	G-C
51747	A-G
52474	C-G
52733	C-A
52875	G-A
53707	G-A
54819	A-G
55913	T-C
56225	A-C
56510	T-C
56566	G-A
56618	A-T
57815	A-G
58011	T DEL
58247-58248	T INS
58926	C-G
59406	C-G
59422	G-C
60221-60222	A INS
60656-60657	CA DEL
61162	G-A
61465	G-A
61607	A DEL
61653	T-C
61794-61795	T INS
62061	G-C
62362	T-G
62732	C-G
63364	G-A
63430-63431	GT INS
63754	C-T

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
63785	A-C
63870-63871	A INS
64788	A-G
64962	G-A
65891	C-T
66675	G-C
67186-67187	ATT INS
67746-67747	TT INS
68259	T-C
68836	T-C
68976	C-G
72508	T-G
72688	C-G
75323-75324	T INS
75887	G-C
77519	T-C
77749	G-A
77908	T-C
78385	C-G
78592-78593	AG INS
80189	T-G
80279	T DEL
80989-80990	A INS
81193	T-C
81273	A DEL
82166	G-A
83847	T DEL
84161-84162	CA-GG
84533	A-G
84638	T-G
85526	T-G
85705	G-T
86984	T-C
87655	T-C
87713	A-C
87892	C-T
88192	T DEL
88528	A-G
89645	A-T
89728	A-G
90088	T-C
91193-91194	2209bp INS
91373	T-C
91433-91434	A INS
91747	G-A
93625	T DEL
95116-95117	T INS
96315	G-A
97981	A-G
98351	T DEL
99249	C-T
100094-1 00095	T INS
100647-100648	TTC INS
100951	C-T

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
101610	C-G
102589	C-T
103076-1 03077	TATATATATATATA INS (SEQ ID NO:19)
103747	T-C
105638	A-C
107024	C-T
107322	C-T
107858	C-G
109019	A DEL
109579	T DEL
110021	C-A
111251	C-A
111425	G-A
112644	T-A
113001	G-C
113130	C-T
114026	G-A
114250	A DEL
115217	C-G
117995	G-A
118874	A-G
119470	T-C
119646	G-T
120853	C-T
121582	G-A
123576	A-C
125581	C-T
125970	G-T
126197	A-G
126672	A DEL
126672	G-C
128220-128221	A INS
132569	C-T
133572	A-C
134064	T-G
136999	G-A
137784	C-T
138903	G-A
1391 59-1 39160	A INS
140359	G-A
140898	C-T
141313	C DEL
141343	T-C
142148	T-C
142178	C-A
142433-1 42434	ATAGA INS
143783	C-T
144090	C-T
144220-144221	A INS
144725	A-C
145732-145733	AAAAAAAAAAAAA INS (SEQ ID NO:20)
147016-147017	CG DEL

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
147021	G-T
147536	T-G
148936	T-A
149061	T-C
154341	A-T
154588	G-A
155464	G-A
158574	C-G
160007	C-T
164348	A-T
164499	C-G
166677-166678	AAAG INS
167389	G-A
168506-168507	AGGATGGTCT INS (SEQ ID NO:21)
168515	T-C
169413-169414	AA INS
170300-170301	TTGTTGTTGTTG INS (SEQ ID NO:22)
170491	G-A
173428	T-C
173642	G-A
173948	T-G
175330	T-C
175836	T-C
176200	G-C
176222	T-C
176524	A-T
176684	G-A
176815	T-C
177049	T-C
177065	G-T
178285	T-C
179114-179115	A INS
179260	C-G
179281	C-G
180023	G-C
180430	T-C
180773	T-C
180824	T-C
181097	C-T
181183	A-T
182351	C-T
183197	G-A
183623	A-T
183653	G-T
183657	T-G
183795-183796	A INS
184060	G-A
184993	G-A
185918	A-G
186036	T-C
186506-186507	TAAC INS
186561-186568	TATTTATT DEL

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
186690	G DEL
186751	T-A
187221	A-G
187260	A-G
187444-187447	CTCT DEL
187831-187832	C INS
188638	G-A
188642	C-T
189246	T-C
190340	A-C
190354	A-G
190762	A-G
191260	G-T
193018-193019	AGAT INS
193147	T-G
193196-193197	C INS
193499	C-T
193738	C-G
193984-193985	ACACACAC INS
194064	C-G
194504	A DEL
194734	G-A
194890	A-C
195404	G-A
195693	A-T
196205	G-A
197424	C-T
197513	C-T
197670	G-A
198055	C-A
198401	C-T
198692	A-G
198780	T DEL
199030	T-G
199933	C-T
200027	G-A
200439	T-A
200452	A-G
200472-200483	AATAATAATAAT DEL (SEQ ID NO:24)
200559	A-T
200745	A-G
200919	T-A
201816	C-T
201861-201862	42bp INS
202662	T-C
202880	T-C
204341	C-T
204768	A-T
205284	T-G
207400	C-A
208634	T-C
208718	T DEL
208862	A-C

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
209419-209420	TT DEL
209802	G-A
209944	C-G
210299	A-G
211142	G-A
212072	G-A
212146	T-C
212379	G-A
212637-212639	TCTDEL
212696	T-C
213042	T-A
214192	A-G
214549	T-C
214795	C-T
214908	T-G
214977	A-G
215769	C-T
215947	C-A
216232	A-G
217478	G-A
219052	T-C
219082-219083	ATATATATATATATATATAT INS
219314	C-A
219327	G-A
219560	C-T
219660	C-T
219889	G-A
220198	G-T
220384	G-A
220451-220452	CAAAAA INS
221363	G-A
221645	G-A
222119	T-C
222358	A-G
222367	A-C
222686	A-G
222959	T-C
223270-223271	TT DEL
223283	T-C
224964	T-C
225232	A-C
225416	G-C
225486	T-C
226088	A-G
228421	A-G
230047	G-A
230109	G-C
230376	C-G
230394	A-C
231226	A-G
231447	G-A
231835	A-G

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
232400-232402	AAA DEL
232402-232403	G INS
232515	G-C
232703	G-T
232750	A-G

70. (New) The isolated polynucleotide of Claim 69, wherein the polymorphic site is at base 61465 of SEQ ID NO:1.

71. (New) The isolated polynucleotide of Claim 69, wherein the polymorphic site is at base 35983 of SEQ ID NO:1.

72. (New) A pair of isolated polynucleotides as in Claim 69.

73. (New) A kit comprising an isolated polynucleotide of Claim 69.

74. (New) A kit comprising at least one pair of isolated polynucleotides as in Claim 72.

75. (New) An isolated polynucleotide comprising at least 18 consecutive bases and up to about 100 consecutive bases of the sequence shown in SEQ ID NOS: 1 or 2, or the complement thereof, wherein said isolated polynucleotide includes at least one polymorphic site selected from the group consisting of polymorphic sites listed in the following table:

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
841	T-C
2662-2663	TT DEL
3767	T-C
3829	C-G
4925-4928	TAAA DEL
5691	C-T
5839	T-C
6011	G-A
6047	C-G
6231	G-A
6643	A DEL
6698	T-C
7186	T-C
7273	G-A
7545-7558	TCACACACCGATTGG DEL (SEQ ID NO:17)
7672	G DEL
7933	T-C
8746	T-G
9115	G-A
9823	G-A
10027	G-A
10214	C-T
10828	A-G
10918	C-G
10955	A-G

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
11524	C-A
11674	A-G
11955	T-C
12173-12175	TTT DEL
13304	G-A
13455	G-A
14416-14417	A INS
14998	C-T
15564	T-C
15887	A-G
15904-1 5919	CCAAACTGATCTTTGA DEL (SEQ ID NO:18)
16019	T DEL
16211	A-T
17461	A-G
19755	G-A
19949	C-T
20085	C-T
20366-20367	A INS
20463	C-A
20841	A-T
21059	A-T
21117	A-G
21837	A-C
22293	A-C
22786	C-A
23009	G-A
24143	T-A
26175	G-C
26667	C-A
26994	T-C
27838	G-T
27861	T DEL
28132	G-A
29100	G-A
29454-29457	TTTT DEL
29787	T-G
29825	A-C
30009	T-C
30177	A-G
30400	A-G
31059	T-A
31280	C-T
31749	C-T
32040	C-G
33017	T-G
33026	T DEL
34434	C-T
35179	A-C
35695	G-A
35702	G-A
35983	A-G
37411	A-G
38526	C-T

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
40431	C-A
42054-42055	TT DEL
43783-43784	TTTT INS
45120	C DEL
45567	A-C
46601	A-T
47255	C-G
47758	C-A
47994	G-C
48440	G-A
48650	T-G
48680	A-G
50240	C-T
50553	G-A
50586	G-T
51322	G-C
51747	A-G
52474	C-G
52733	C-A
52875	G-A
53707	G-A
54819	A-G
55913	T-C
56225	A-C
56510	T-C
56566	G-A
56618	A-T
57815	A-G
58011	T DEL
58247-58248	T INS
58926	C-G
59406	C-G
59422	G-C
60221-60222	A INS
60656-60657	CA DEL
61162	G-A
61465	G-A
61607	A DEL
61653	T-C
61794-61795	T INS
62061	G-C
62362	T-G
62732	C-G
63364	G-A
63430-63431	GT INS
63754	C-T
63785	A-C
63870-63871	A INS
64788	A-G
64962	G-A
65891	C-T
66675	G-C
67186-67187	ATT INS
67746-67747	TT INS

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
68259	T-C
68836	T-C
68976	C-G
72508	T-G
72688	C-G
75323-75324	T INS
75887	G-C
77519	T-C
77749	G-A
77908	T-C
78385	C-G
78592-78593	AG INS
80189	T-G
80279	T DEL
80989-80990	A INS
81193	T-C
81273	A DEL
82166	G-A
83847	T DEL
84161-84162	CA-GG
84533	A-G
84638	T-G
85526	T-G
85705	G-T
86984	T-C
87655	T-C
87713	A-C
87892	C-T
88192	T DEL
88528	A-G
89645	A-T
89728	A-G
90088	T-C
91193-91194	2209bp INS
91373	T-C
91433-91434	A INS
91747	G-A
93625	T DEL
95116-95117	T INS
96315	G-A
97981	A-G
98351	T DEL
99249	C-T
100094-1 00095	T INS
100647-100648	TTC INS
100951	C-T
101610	C-G
102589	C-T
103076-1 03077	TATATATATATATA INS (SEQ ID NO:19)
103747	T-C
105638	A-C
107024	C-T
107322	C-T

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
107858	C-G
109019	A DEL
109579	T DEL
110021	C-A
111251	C-A
111425	G-A
112644	T-A
113001	G-C
113130	C-T
114026	G-A
114250	A DEL
115217	C-G
117995	G-A
118874	A-G
119470	T-C
119646	G-T
120853	C-T
121582	G-A
123576	A-C
125581	C-T
125970	G-T
126197	A-G
126672	A DEL
126672	G-C
128220-128221	A INS
132569	C-T
133572	A-C
134064	T-G
136999	G-A
137784	C-T
138903	G-A
1391 59-1 39160	A INS
140359	G-A
140898	C-T
141313	C DEL
141343	T-C
142148	T-C
142178	C-A
142433-1 42434	ATAGA INS
143783	C-T
144090	C-T
144220-144221	A INS
144725	A-C
145732-145733	AAAAAAAAAAAAA INS (SEQ ID NO:20)
147016-147017	CG DEL
147021	G-T
147536	T-G
148936	T-A
149061	T-C
154341	A-T
154588	G-A
155464	G-A
158574	C-G

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
160007	C-T
164348	A-T
164499	C-G
166677-166678	AAAG INS
167389	G-A
168506-168507	AGGATGGTCT INS (SEQ ID NO:21)
168515	T-C
169413-169414	AA INS
170300-170301	TTGTTGTTGTTG INS (SEQ ID NO:22)
170491	G-A
173428	T-C
173642	G-A
173948	T-G
175330	T-C
175836	T-C
176200	G-C
176222	T-C
176524	A-T
176684	G-A
176815	T-C
177049	T-C
177065	G-T
178285	T-C
179114-179115	A INS
179260	C-G
179281	C-G
180023	G-C
180430	T-C
180773	T-C
180824	T-C
181097	C-T
181183	A-T
182351	C-T
183197	G-A
183623	A-T
183653	G-T
183657	T-G
183795-183796	A INS
184060	G-A
184993	G-A
185918	A-G
186036	T-C
186506-186507	TAAC INS
186561-186568	TATTTATT DEL
186690	G DEL
186751	T-A
187221	A-G
187260	A-G
187444-187447	CTCT DEL
187831-187832	C INS
188638	G-A
188642	C-T

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
189246	T-C
190340	A-C
190354	A-G
190762	A-G
191260	G-T
193018-193019	AGAT INS
193147	T-G
193196-193197	C INS
193499	C-T
193738	C-G
193984-193985	ACACACAC INS
194064	C-G
194504	A DEL
194734	G-A
194890	A-C
195404	G-A
195693	A-T
196205	G-A
197424	C-T
197513	C-T
197670	G-A
198055	C-A
198401	C-T
198692	A-G
198780	T DEL
199030	T-G
199933	C-T
200027	G-A
200439	T-A
200452	A-G
200472-200483	AATAATAATAAT DEL (SEQ ID NO:24)
200559	A-T
200745	A-G
200919	T-A
201816	C-T
201861-201862	42bp INS
202662	T-C
202880	T-C
204341	C-T
204768	A-T
205284	T-G
207400	C-A
208634	T-C
208718	T DEL
208862	A-C
209419-209420	TT DEL
209802	G-A
209944	C-G
210299	A-G
211142	G-A
212072	G-A
212146	T-C
212379	G-A

POLYMORPHIC SITE IN SEQ ID NO:1	POLYMORPHISM
212637-212639	TCTDEL
212696	T-C
213042	T-A
214192	A-G
214549	T-C
214795	C-T
214908	T-G
214977	A-G
215769	C-T
215947	C-A
216232	A-G
217478	G-A
219052	T-C
219082-219083	ATATATATATATATATATAT INS
219314	C-A
219327	G-A
219560	C-T
219660	C-T
219889	G-A
220198	G-T
220384	G-A
220451-220452	CAAAAA INS
221363	G-A
221645	G-A
222119	T-C
222358	A-G
222367	A-C
222686	A-G
222959	T-C
223270-223271	TT DEL
223283	T-C
224964	T-C
225232	A-C
225416	G-C
225486	T-C
226088	A-G
228421	A-G
230047	G-A
230109	G-C
230376	C-G
230394	A-C
231226	A-G
231447	G-A
231835	A-G
232400-232402	AAA DEL
232402-232403	G INS
232515	G-C
232703	G-T
232750	A-G

76. (New) The isolated polynucleotide of Claim 75, wherein the polymorphic site is at base 61465 of SEQ ID NO:1.

77. (New) The isolated polynucleotide of Claim 75, wherein the polymorphic site is at base 35983 of SEQ ID NO:1.

78. (New) A pair of isolated polynucleotides as in Claim 75.

79. (New) A kit comprising an isolated polynucleotide of Claim 75.